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RAW SEQUENCE LISTING PATENT APPLICATION US/08/981,087A

DATE: 09/24/1999

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This Raw Listing contains the General Information Section and up to the first 5 pages.

ENTERED

| 1 | | SEQUENCE LISTING |
|-----------------------|--------|--|
| 2 3 | (1) G | eneral Information: |
| 4 | (1) | chorar Información. |
| 5 6 7 8 9 | (i) | APPLICANT: Elmore, Michael J. Mauchline, Margaret L. Minton, Nigel P. Pasechnik, Vladimir A. Titball, Richard W. |
| 11 | (ii) | TITLE OF INVENTION: TYPE F BOTULINUM TOXIN AND USE THEREOF |
| 12 | (11) | TITLE OF INVENTION. THE PROPERTY OF THE MEDICAL PROPERTY OF THE MEDICAL PROPERTY OF THE PROPER |
| 13 | (iii) | NUMBER OF SEQUENCES: 6 |
| 14 | ν | |
| 15 | (iv) | CORRESPONDENCE ADDRESS: |
| 16 | | (A) ADDRESSEE: NIXON & VANDERHYE P.C. |
| 17 | | (B) STREET: 1100 North Glebe Rd. 8th floor |
| 18 | | (C) CITY: Arlington |
| 19 | | (D) STATE: VA |
| 20 | | (E) COUNTRY: USA |
| 21 | | (F) ZIP: 22201-4741 |
| 22 | | |
| 23 | (v) | COMPUTER READABLE FORM: |
| 24 | | (A) MEDIUM TYPE: Floppy disk |
| 25 | | (B) COMPUTER: IBM PC compatible |
| 26 | | (C) OPERATING SYSTEM: PC-DOS/MS-DOS |
| 27 | | (D) SOFTWARE: PatentIn Release #1.0, Version #1.30 |
| 28 29 | (i \ | CURRENT APPLICATION DATA: |
| 30 | (VI) | (A) APPLICATION NUMBER: US 08/981,087 |
| 31 | | (B) FILING DATE: 27-MAY-1998 |
| 32 | | (C) CLASSIFICATION: |
| 33 | | (C) CLABBITICATION. |
| 34 | (vii) | PRIOR APPLICATION DATA: |
| 35 | (/ | (A) APPLICATION NUMBER: PCT/GB96/01409 |
| 36 | | (B) FILING DATE: 12-JUN-1996 |
| 37 | • | • • |
| 38 | (vii) | PRIOR APPLICATION DATA: |
| 39 | | (A) APPLICATION NUMBER: GB 9511909.5 |
| 40 | | (B) FILING DATE: 12-JUN-1995 |
| 41 | | |
| 42 | (viii) | ATTORNEY/AGENT INFORMATION: |
| 43 | | (A) NAME: Crawford, Arthur R. |
| 44 | | (B) REGISTRATION NUMBER: 25,327 |
| 45 | | (C) PEEEPENCE/DOCKET NIMPED, 124_600 |

RAW SEQUENCE LISTING PATENT APPLICATION US/08/981,087A

DATE: 09/24/1999 TIME: 15:58:49

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| 47 48 49 50 51 | | (ix) | (A |) TE | LEPH | ONE: | | -816 | MATI -400 | | | | | INI | PUI S | EI: S | 334/1.1 | |
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| 52 | (2) | INFO | RMAT | ION : | FOR a | SEQ : | ID N | 0:1: | | | | | | | | | | |
| 53 54 55 56 57 58 59 | | (i) | (A (B (C | SEQUENCE CHARACTERISTICS: (A) LENGTH: 431 amino acids (B) TYPE: amino acid (C) STRANDEDNESS: (D) TOPOLOGY: linear | | | | | | | | | | | | | | |
| 60 61 62 63 | | (ii) | MOL | MOLECULE TYPE: peptide | | | | | | | | | | | | | | |
| 6 4 65 | | (xi) | SEQ | UENC | E DE | SCRI | PTIO | N: S | EQ I | on o | :1: | | | | | | | |
| 66 67 68 69 | | Ser 1 | Tyr | Thr | Asn | Asp 5 | Lys | Ile | Leu | Ile | Leu 10 | Tyr | Phe | Asn | Lys | Leu 15 | Tyr | |
| 70 71 72 | | Lys | Lys | Ile | Lys 20 | Asp | Asn | Ser | Ile | Leu 25 | Asp | Met | Arg | Tyr | Glu 30 | Asn | Asn | |
| 73 74 75 | | Lys | Phe | Ile 35 | Asp | Ile | Ser | Gly | Tyr 40 | Gly | Ser | Asn | Ile | Ser 45 | Ile | Asn | Gly | |
| 76 77 78 | | Asp | Val 50 | Tyr | Ile | Tyr | Ser | Thr 55 | Asn | Arg | Asn | Gln | Phe 60 | Gly | Ile | Tyr | Ser | |
| 79 80 81 | | 65 | _ | | | | 70 | | | | Gln | 75 | | _ | | | 80 | |
| 82 83 84 | | | | | | 85 | | | | | Ser 90 | • | | | | 95 | | |
| 85 86 87 | | | | | 100 | | | | | 105 | Asn | | _ | | 110 | | _ | |
| 88 89 90 | | | | 115 | | | | | 120 | | Lys | | | 125 | | | | |
| 91 92 93 | | Lys | Ile 130 | Ile | Trp | Thr | Leu | Gln 135 | Asp | Thr | Ala | Gly | Asn 140 | Asn | Gln | Lys | Leu | |
| 94 95 96 | | 145 | | | | | 150 | | | | Ile | 155 | | | | | 160 | |
| 97 98 99 | | Trp | Ile | Phe | Val | Thr 165 | Ile | Thr | Asn | Asn | Arg 170 | Leu | Gly | Asn | Ser | Arg 175 | Ile | |

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DATE: 09/24/1999 TIME: 15:58:50

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| | | | | | | | | | | | | | | INPUT SET: S33471.raw | | | | | |
| 100 | | Tyr | Ile | Asn | Gly | Asn | Leu | Ile | Asp | Glu | Lys | Ser | Ile | | | | Gly | | |
| 101 | | | | | 180 | | | | | 185 | | | | | 190 | | | | |
| 102 | | | | | | | | | | | | | | | | | | | |
| 103 | | Asp | Ile | His | Val | Ser | Asp | Asn | Ile | Leu | Phe | Lys | Ile | Val | Gly | Cys | Asn | | |
| 104 | | | | 195 | | | | | 200 | | | | | 205 | | | | | |
| 105 | | | | | | | | | | | | | | | | | | | |
| 106 | | Asp | | Arg | Tyr | Val | Gly | Ile | Arg | Tyr | Phe | Lys | Val | Phe | Asp | Thr | Glu | | |
| 107 | | | 210 | | | | | 215 | | | | | 220 | | | | | | |
| 108 | | | | | | | | | | | | | | | | | | | |
| 109 | | | Gly | Lys | Thr | Glu | | Glu | Thr | Leu | Tyr | | Asp | Glu | Pro | Asp | Pro | | |
| 110 | | 225 | | | | | 230 | | | | | 235 | | | | | 240 | | |
| 111 | | _ | | _ | _ | _ | | | | | | | _ | | | | | | |
| 112 | | Ser | Ile | Leu | Lys | | Phe | Trp | Gly | Asn | | Leu | Leu | Tyr | Asn | | Arg | | |
| 113 | | | | | | 245 | | | | | 250 | | | | | 255 | | | |
| 114 | | _ | _ | _ | _ | _ | _ | _ | _ | _, | _ | _ | _ | | | | | | |
| 115 | | Tyr | Tyr | Leu | | Asn | Leu | Leu | Arg | | Asp | ьуs | ser | IIe | | GIn | Asn | | |
| 116 | | | | | 260 | | | | | 265 | | | | | 270 | | | | |
| 117 | | 0 | 7 | nh- | T | 2 | T1. | 3 | ~1 ~ | a1 | 7 | a 1 | 77 7 | | ~1 | T | D | | |
| 118 | | ser | ASII | | Leu | ASII | тте | ASII | Gln | GIN | Arg | GIY | vaı | _ | GIN | гÃг | Pro | | |
| 119 120 | | | | 275 | | | | | 280 | | | | | 285 | | | | | |
| 121 | | Λαn | т1 о | Dhe | Car | λαη | Thr | 7 ~~ | Leu | Ф | Thr | C111 | v-1 | ~1., | v-1 | т1- | Tlo | | |
| 122 | | ASII | 290 | FILE | PET | HSII | 1111 | 295 | пеп | TAT | 1111 | СТУ | 300 | GIU | vaı | TIE | TIE | | |
| 123 | | | 230 | | | | | 295 | | | | | 300 | | | | | | |
| 124 | | Ara | Lvs | Asn | Glv | Ser | Thr | Asp | Ile | Ser | Δsn | Thr | Asn | Δsn | Phe | Va 1 | Δrσ | | |
| 125 | | 305 | - 175 | 11011 | 017 | 501 | 310 | nop | | 501 | T.D.II | 315 | TOP | AUII | 1110 | Val | 320 | | |
| 126 | | 505 | | | | | 010 | | | | | 323 | | | | | 320 | | |
| 127 | | Lvs | Asn | Asp | Leu | Ala | Tvr | Ile | Asn | Val | Val | Asp | Ara | Asp | Val | Glu | Tvr | | |
| 128 | | • | | - | | 325 | • | | | | 330 | | , | | | 335 | -1- | | |
| 129 | | | | | | | | | | | | | | | | | | | |
| 130 | | Arg | Leu | Tyr | Ala | Asp | Ile | Ser | Ile | Ala | Lys | Pro | Glu | Lys | Ile | Ile | Lys | | |
| 131 | | _ | | _ | 340 | _ | | | | 345 | - | | | - | 350 | | - | | |
| 132 | | | | | | | | | | | | | | | | | | | |
| 133 | | Leu | Ile | Arg | Thr | Ser | Asn | Ser | Asn | Asn | Ser | Leu | Gly | Gln | Ile | Ile | Val | | |
| 134 | | | | 355 | | | | | 360 | | | | | 365 | | | | | |
| 135 | | | | | | | | | | | | 7 | | | | | | | |
| 136 | | Met | Asp | Ser | Ile | Gly | Asn | Asn | Cys | Thr | Met | Asn | Phe | Gln | Asn | Asn | Asn | | |
| 137 | | | 370 | | | | | 375 | | | | | 380 | | | | | | |
| 138 | | _ | _ | | | | | | _ | | | | | | | | | | |
| 139 | | _ | Gly | Asn | Ile | Gly | | Leu | Gly | Phe | His | | Asn | Asn | Leu | Val | | | |
| 140 | | 385 | | | | | 390 | | | | | 395 | | | | | 400, | | |
| 141 | | _ | _ | _ | | _ | _ | _ | | _ | _ | _ | | _ | _ | | | | |
| 142 | | Ser | Ser | Trp | Tyr | | Asn | Asn | Ile | Arg | | Asn | Thr | Ser | Ser | | Gly | | |
| 143 | | | | | | 405 | | | | | 410 | | | | | 415 | | | |
| 144 | | a | D1 | m- | | -1 | -7. | a | T | ~ ? | ••• | ~~ | - | ~ 3 | ~ 3 | • | | | |
| 145 | | Cys | Pne | Trp | | Phe | Ile | ser | Lys | | His | GŢŻ | Trp | Gin | | Asn | | | |
| 146 | | | | | 420 | | | | | 425 | | | | | 430 | | | | |
| 147 | (2) | TNECT | יייו אואר | | 70E 1 | 100 - | | 3.2 | | | | | | | | | | | |
| 148 149 | (2) | INFO | CMA.I. | rOM] | OR S | PEQ . | א מו | J:∠: | | | | | | | | | | | |
| 150 | | (4) | QEO! | TERTOT | ייים ק | יים א כו ו | י ד מימיו | 277700 | z . | | | | | | | | | | |
| 120 | | (1) | DEQ! | וטמפי | a CHA | ARACT | FEKT | 5 I T C S |) ; | | | | | | | | | | |

(i) SEQUENCE CHARACTERISTICS.

(A) LENGTH: 144 amino acids

(B) TYPE: amino acid 150 151

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DATE: 09/24/1999 TIME: 15:58:50

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| 153 | | (C |) ST | RAND: | EDNE | SS: | | | | | | | INI | PUT S | ET: S | 33471. |
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| 154 | | (D |) TO: | POLO | GY: | line | ar | | | | | | | | | |
| 155 | | | | | | | | | | | | | | | | |
| 156 | (ii) | MOL | ECUL: | E TY | PE:] | pept: | ide | | | | | | | | | |
| 157 | | | | | | | | | | | | | | | | |
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| 159 | | | | | | | | | | | | | | | | |
| 160 | | | | | | | | | | | | | | | | |
| 161 | (xi) | SEQ | UENC: | E DE | SCRI | PTIO | 1: S | EQ I | D NO | :2: | | | | | | |
| 162 | _ | _ | | _ | _ | _ | | _ | | _ | _ | | | | | _ |
| 163 | | Tyr | Thr | Asn | _ | Lys | Ile | Leu | Ile | | Tyr | Phe | Asn | Lys | | \mathtt{Tyr} |
| 164 | 1 | | | | 5 | | | | | 10 | | | | | 15 | |
| 165 | _ | _ | | _ | _ | _ | _ | | _ | _ | | _ | _ | | _ | _ |
| 166 | Lys | Lys | Ile | _ | Asp | Asn | Ser | IIe | | Asp | Met | Arg | Tyr | | Asn | Asn |
| 167 | | | | 20 | | | | | 25 | | | | | 30 | | |
| 168 | _ | _, | | _ | | _ | ~-7 | _ | ~ 7 | _ | _ | | _ | | _ | ~-7 |
| 169 | Lys | Phe | | Asp | тте | ser | GIY | | GIĀ | Ser | Asn | IIe | | TTE | Asn | GIY |
| 170 | | | 35 | | | | | 40 | | | | | 45 | | | |
| 171 | - | 3 | _ | -1- | _ | | 1 | | | _ | ~7 - | | ~7 | -1. | _ | ~ |
| 172 | Asp | Val | Tyr | тте | Tyr | ser | | Asn | Arg | Asn | GIN | | GLY | тте | Tyr | ser |
| 173 | | 50 | | | | | 55 | | | | | 60 | | | | |
| 174 | a | - | 5 | a | ~1 | *** 7 | • | -1 - | | a1 | • | • | • | -1- | -1- | m |
| 175 | | Lys | Pro | ser | GIU | | Asn | тте | Ата | Gin | | Asn | Asp | IIe | IIе | |
| 176 | 65 | | | | | 70 | | | | | 75 | | | | | 80 |
| 177 | 7 | a 1 | 7 | m | ~1 - | 7 | Dh.a | a | T 1. | C | Db - | | 77. 7 | 3 | - 1. | D |
| 178 | Asn | Gly | Arg | Tyr | | ASI | Pne | ser | iie | | Pne | Trp | vaı | Arg | | Pro |
| 179 | | | | | 85 | | | | | 90 | | | | | 95 | |
| 180 | ¥ | m | Dh. | 3 | T | 17. 7 | 3 | T | 3 | 3 | ~ 1 | | m\ | | 7 1. | 3 |
| 181 | ьys | Tyr | Pne | | гуѕ | vai | ASII | ьeu | | ASI | GIU | Tyr | Thr | | тте | Asp |
| 182 | | | | 100 | | | | | 105 | | | | | 110 | | |
| 183 184 | Crra | Ile | 7 ~~~ | 7 an | 7 0 0 | 7 an | C0~ | ~1·· | m~~ | T | T1. | 000 | T 011 | 7 | M= ==0 | 7.00 |
| 185 | СуБ | 116 | 115 | ASII | ASII | ASII | Ser | 120 | тър | пуъ | TIE | per | 125 | ASII | ıyı | ASII |
| 186 | | | 113 | | | | | 120 | | | | | 125 | | | |
| 187 | Lare | Ile | т1Д | Trn | Thr | T.011 | Gln | Nen | Thr | λ1 ₂ | Gl ₃ | λen | λen | Gln | Laze | T.011 |
| 188 | цуз | 130 | 110 | тър | 1111 | Цец | 135 | ASP | 1111 | AIA | Gry | 140 | VOII | GIII | цуэ | пеа |
| 189 | | 130 | | | | | 133 | | | | | 140 | | | | |
| 190 | | | | | | | | | | | | | | | | |
| 191 | (2) INFO | RMATT. | ION 1 | FOR 9 | SEO : | א מז |):3. | | | | | | | | | |
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| 193 | (i) | SEQ | JENCI | е сна | ARAC | PERT | STICS | 3: | | | | | | | | |
| 194 | (-) | - | | | : 144 | | | | 3 | | | | | | | |
| 195 | | | | | amino | | | | | | | | | | | |
| 196 | | | | | EDNES | | | | | | | | | | | |
| 197 | | | | | GY: | | ar | | | | | | | | | |
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| 199 | (ii) | MOLI | ECULI | TY | PE: r | ept: | ide | | | | | | | | | |
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| 203 | | | | | | | | | | | | | | | | |
| 204 | (xi) | SEQ | JENCI | E DES | SCRII | OITS | V: SI | EO II | NO: | : 3 : | | | | | | |
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| 206 | | | Phe | Asn | Tyr | | Gln | Met | Ile | Ser | | Ser | Asp | Tyr | Ile | | Lys |
| 207 | | 1 | | | | 5 | | | | | 10 | | | | | 15 | |
| 208 209 | | Tro | Tle | Phe | Val | Thr | Tle | Thr | Asn | Asn | Ara | Leu | Glv | Asn | Ser | Ara | Tle |
| 210 | | 115 | | 1110 | 20 | | | | 11011 | 25 | 9 | | 017 | 71011 | 30 | Ar 9 | 110 |
| 211 | | | | | | | | | | | | | | | | | |
| 212 | | Tyr | Ile | Asn | Gly | Asn | Leu | Ile | Asp | Glu | Lys | Ser | Ile | Ser | Asn | Leu | Gly |
| 213 | | | | 35 | | | | | 40 | | | | | 45 | | | |
| 214 | | _ | | ' | - | _ | _ | _ | | _ | | _ | | | · | _ | |
| 215 | | Asp | | His | Val | Ser | Asp | | IIe | Leu | Phe | Lys | | Val | GLY | Cys | Asn |
| 216 217 | | | 50 | | | | | 55 | | | | | 60 | | | | |
| 217 | | Asp | Thr | Arg | Tvr | ٧al | Glv | Tle | Ara | Tvr | Phe | Lvs | Val | Phe | Δsn | Thr | Glu |
| 219 | | 65 | | 9 | -1- | | 70 | | 9 | -1- | | 75 | • • • • | | 1100 | **** | 80 |
| 220 | | | | | | | | | | | | | | | | | |
| 221 | | Leu | Gly | Lys | Thr | Glu | Ile | Glu | Thr | Leu | Tyr | Ser | Asp | Glu | Pro | Asp | Pro |
| 222 | | | | | | 85 | | | | | 90 | | | | | 95 | |
| 223 | | _ | | _ | _ | _ | | _ | | _ | _ | | | | | | |
| 224 | | Ser | Ile | Leu | | Asp | Phe | Trp | GIY | | Tyr | Leu | Leu | Tyr | | Lys | Arg |
| 225 226 | | | | | 100 | | | | | 105 | | | | | 110 | | |
| 227 | | ጥኒ/ | Туг | Leu | I.Q11 | Δen | T.@11 | T.A11 | Δrα | Thr | Δen | Lve | Sor | т1Д | Thr | Gln. | Aen |
| 228 | | - 7 - | - 7 - | 115 | шец | AUII | пси | LCu | 120 | | пор | цуз | ber | 125 | 1111 | GIII | ASII |
| 229 | | | | | | | | | | | | | | | | | |
| 230 | | Ser | Asn | Phe | Leu | Asn | Ile | Asn | Gln | ${\tt Gln}$ | Arg | Gly | Val | Tyr | Gln | Lys | Pro |
| 231 | | | 130 | | | | | 135 | | | | | 140 | | | | |
| 232 | | | | | | | | | | | | | | | | | |
| 233 | (0) | TNEO | 388 m | | 70D (| | FD 37/ | | | | | | | | | | |
| 234 235 | (2) | INFO | WAT. | LOM 1 | OR : | EQ. | או עו |):4: | | | | | | | | | |
| 236 | | (i) | SEO | JENCE | E CHA | ARACT | FRTS | STICS | 3: | | | | | | | | |
| 237 | | (-/ | |) LEI | | | | | | 3 | | | | | | | |
| 238 | | | (B) | TYI | PE: 6 | amino | ac | id | | | | | | | | | , |
| 239 | | | (C) | STI | RANDI | EDNES | SS: | | | | | | | | | | |
| 240 | | | (D) | TOI | POLO | 3Y:] | linea | ar | | | | | | | | | |
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| 242 | | (ii) | MOLI | 5CULI | r TYI | E: I | pepti | Lae | | | | | | | | | |
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| 247 | | (xi) | SEQU | JENCE | DES | CRI | OITS | 1: SI | EQ II | NO: | 4: | | | | | | |
| 248 | | | | | | | | | | | | | | | | | |
| 249 | | | Ile | Phe | Ser | | Thr | Arg | Leu | Tyr | | Gly | Val | Glu | Val | | Ile |
| 250 | | 1 | | | | 5 | | | | | 10 | | | | | 15 | |

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